

CLAIMS

1. A liposome modified by a sugar chain bonded to the membrane of the liposome.
2. The liposome modified by a sugar chain according to claim 1, wherein a constitutional lipid of the liposome comprises phosphatidylcholines (0 to 70% by mole), phosphatidylethanolamines (0 to 30% by mole); not less than one lipid (0 to 30% by mole) selected from the group consisting of phosphatidic acids, long-chain alkyl phosphates and dicetyl phosphates; not less than one lipid (0 to 40% by mole) selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, and sphingomyelins; and cholesterol (0 to 70% by mole).
3. The liposome modified by a sugar chain according to claim 2, wherein the at least one lipid selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, sphingomyelins and cholesterol gathers on the surface of the liposome to form a raft.
4. The liposome modified by a sugar chain according to any one of claims 1 to 3, wherein the sugar chain controlled in type and density is bonded.
5. The liposome modified by a sugar chain according to any one of claims 1 to 4, wherein the liposome has a particle diameter of 30 to 500 nm.
6. The liposome modified by a sugar chain according to claim 5, wherein the liposome has a particle diameter of 50 to 350 nm.
7. The liposome modified by a sugar chain according to any one of claims 1 to 6, wherein the liposome has a zeta potential of -50 to 10 mV.
8. The liposome modified by a sugar chain according to claim 7, wherein the liposome has a zeta potential of -40 to 0 mV.
9. The liposome modified by a sugar chain according to claim 8, wherein the liposome has a zeta potential of -30 to -10 mV.
10. The liposome modified by a sugar chain according to any one of claims 1 to 9, wherein the sugar chain is bonded to the membrane of the liposome via a linker protein.

11. The liposome modified by a sugar chain according to claim 10, wherein the linker protein is a protein derived from the living body.

12. The liposome modified by a sugar chain according to claim 11, wherein the linker protein is a protein derived from a human.

13. The liposome modified by a sugar chain according to claim 12, wherein the linker protein is a human serum protein.

14. The liposome modified by a sugar chain according to claim 11, wherein the linker protein is human serum albumin or bovine serum albumin.

15. The liposome modified by a sugar chain according to any one of claims 1 to 14, wherein the linker protein is bonded onto a raft formed of at least one lipid selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, sphingomyelins and cholesterol formed on the surface of the liposome.

16. The liposome modified by a sugar chain according to any one of claims 1 to 15, hydrophilized by binding a hydrophilic compound to the membrane of the liposome and/or the linker protein.

17. The liposome modified by a sugar chain according to claim 16, wherein the hydrophilic compound is a low molecular weight substance.

18. The liposome modified by a sugar chain according to claim 16 or 17, wherein the hydrophilic compound rarely causes steric hindrance to the sugar chain and does not prevent proceeding of a reaction of recognizing the sugar chain by a lectin on the membrane surface of a target cell.

19. The liposome modified by a sugar chain according to any one of claims 16 to 18, wherein the hydrophilic compound has a hydroxide group.

20. The liposome modified by a sugar chain according to any one of claims 16 to 19, wherein the hydrophilic compound is an amino alcohol.

21. The liposome modified by a sugar chain according to any one of claims 16 to 20, wherein the hydrophilic compound binds directly to the surface of the liposome membrane.

22. The liposome modified by a sugar chain according to claim 16, hydrophilized by a hydrophilic compound, wherein the hydrophilic compound is represented by the general formula (1):



where R1 denotes a C1 to C40 linear or branched hydrocarbon chain; R2 is absent or represents a C1 to C40 linear or branched hydrocarbon chain; X represents a reactive functional group directly binding to a liposome lipid or a linker protein, or binding to a divalent crosslinking agent; and n is a natural number.

23. The liposome modified by a sugar chain according to claim 16, hydrophilized by a hydrophilic compound, wherein the hydrophilic compound is represented by the general formula (2):



where R3 denotes a C1 to C40 linear or branched hydrocarbon chain; R4 is absent or represents a C1 to C40 linear or branched hydrocarbon chain; H₂N represents a reactive functional group directly binding to a liposome lipid or a linker protein, or binding to a divalent crosslinking agent; and n is a natural number.

24. The liposome modified by a sugar chain according to claim 16, hydrophilized by a hydrophilic compound, wherein the hydrophilic compound is represented by the general formula (3):



where R5 denotes a C1 to C40 straight and branched hydrocarbon chain; H₂N represents a reactive functional group directly binding to a liposome lipid or a linker protein, or binding to a divalent crosslinking agent; and n is a natural number.

25. The liposome modified by a sugar chain according to claim 16, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound being a tris(hydroxyalkyl)aminoalkane to the membrane of the liposome and/or the linker protein.

26. The liposome modified by a sugar chain according to claim 16, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding,

to the membrane of the liposome and/or the linker protein, a hydrophilic compound selected from the group consisting of tris(hydroxymethyl)aminoethane, tris(hydroxyethyl)aminoethane, tris(hydroxypropyl)aminoethane, tris(hydroxymethyl)aminomethane, tris(hydroxyethyl)aminomethane, tris(hydroxypropyl)aminomethane, tris(hydroxymethyl)aminopropane, tris(hydroxyethyl)aminopropane, and tris(hydroxypropyl)aminopropane.

27. The liposome modified by a sugar chain according to any one of claims 1 to 26, wherein the liposome modified by a sugar chain is targeted to a lectin selected from the group consisting of a selectin, DC-SIGN, DC-SIGNR, a C-type lectin including collectin and mannose binding lectin, an I-type lectin including siglec, a P-type lectin including a mannose-6-phosphate receptor, an R-type lectin, an L-type lectin, an M-type lectin, and galectin, all serving as a receptor present on the cellular membrane of each tissue.

28. The liposome modified by a sugar chain according to claim 27, wherein the liposome modified by a sugar chain is targeted to a selectin selected from the group consisting of E-selectin, P-selectin, and L-selectin.

29. The liposome modified by a sugar chain according to any one of claims 1 to 28, wherein a binding density of the sugar chain bonded to the liposome is 1 to 30000 per liposome particle when the linker protein is used, and 1 to 500000 per liposome particle when the linker protein is not used.

30. The liposome modified by a sugar chain according to any one of claims 1 to 28, wherein a binding density of the sugar chain bonded to the liposome is 1 to 60 per protein molecule to be bonded to the liposome.

31. The liposome modified by a sugar chain according to any one of claims 1 to 30, wherein the liposome is capable of being absorbed from the intestinal tract.

32. The liposome modified by a sugar chain according to any one of claims 1 to 31, having high targetability to a tissue or an organ selected from the group consisting of blood, liver, spleen, lung, brain, small intestinal tract, heart, thymus gland, kidney, pancreas, muscle, large intestinal tract, bone, bone marrow, eyes, cancer tissue, inflammatory tissue and lymph node.

33. The liposome modified by a sugar chain according to any one of claims 1 to 32, wherein the sugar chain is bonded to the membrane of the liposome and selected from the group consisting of α -1,2-mannobiose disaccharide, α -1,3-mannobiose disaccharide, α -1,4-mannobiose disaccharide, α -1,6-mannobiose disaccharide, α -1,3/ α -1,6-mannotriose trisaccharide, oligomannose-3 pentasaccharide, oligomannose-4b hexasaccharide, oligomannose-5 heptasaccharide, oligomannose-6 octasaccharide, oligomannose-7 nonasaccharide, oligomannose-8 decasaccharide, and oligomannose-9 undecasaccharide, 3'-sialyllactose trisaccharide, 6'-sialyllactose trisaccharide, 3'-sialyllactosamine trisaccharide, 6'-sialyllactosamine trisaccharide, Lewis X trisaccharide, sialyl Lewis X tetrasaccharide, lactose disaccharide, 2'-fucosyllactose trisaccharide, difucosyllactose tetrasaccharide, and 3-fucosyllactose trisaccharide.

34. A liposome preparation prepared by encapsulating a medicinal drug or a gene in the liposome according to any one of claims 1 to 33.

35. The liposome preparation according to claim 34, wherein the medicinal drug is selected from the group consisting of medicinal drugs for tumors such as an anticancer drug based on an alkylating compound, metabolic antagonist, plant derived anticancer drug, anticancer antibiotic, BRM, cytokine, anticancer drug based on a platinum complex, immunotherapeutic drug, hormonal anticancer drug, and monoclonal antibody; medicinal drugs for the central nerve; medicinal drugs for the peripheral nervous system/sensory organ; therapeutic drugs for a respiratory disease; medicinal drugs for a circulatory organ; medicinal drugs for a digestive organ; hormonal medicinal drugs; medicinal drugs for a urinary/genital organ; medicinal drugs for external application; vitamins/analeptics; medicinal drugs for blood and body fluid; metabolic medicine; antibiotic/chemotherapeutic agents; medicinal drugs for medical check; anti-inflammatory agents; medicinal drugs for eye disorder; medicinal drugs for the central nervous system; medicinal drugs for the autoimmune system; medicinal drugs for the circulatory organ; medicinal drugs for lifestyle-related diseases such as diabetes and hyperlipemia; various oral, pulmonary, transdermal or transmucosal drugs; adenocortical hormones; immunosuppressive agents; antibiotics; anti-viral agents; neovascularization inhibitors; cytokines; chemokines; anti-cytokine antibodies; anti-chemokine antibodies;

anti-cytokine/chemokine receptor antibodies; nucleic acid preparations involved in gene therapy such as siRNA, miRNA, smRNA, antisense ODN and DNA; neuroprotective factors; and various antibody medicines.

36. The liposome preparation according to claim 34 or 35, which is an oral preparation.

37. The liposome preparation according to claim 34 or 35, which is a parenteral preparation.

38. The liposome preparation according to claim 35, wherein the medicinal drug comprising a liposome modified by a sugar chain is doxorubicin.

39. An anticancer drug comprising the liposome preparation according to claim 35, wherein the medicinal drug is a drug for a tumor.

40. The anticancer drug according to claim 39 which is to be orally administered.

41. The anticancer drug according to claim 39 which is to be parenterally administered.

42. A liposome whose membrane is hydrophilized and which has no sugar chain bonded onto surface thereof.

43. The liposome according to claim 42, wherein a constitutional lipid of the liposome comprises phosphatidylcholines (0 to 70% by mole), phosphatidylethanolamines (0 to 30% by mole); not less than one lipid (0 to 30% by mole) selected from the group consisting of phosphatidic acids, long-chain alkyl phosphates and dicetyl phosphates; not less than one lipid (0 to 40% by mole) selected from the group consisting of gangliosides, glycolipids, phosphatidylglycerols, and sphingomyelins; and cholesterol (0 to 70% by mole).

44. The liposome according to claim 42 or 43, further comprising a protein.

45. The liposome according to any one of claims 42 to 44, wherein the membrane of the liposome and/or the linker protein are hydrophilized by binding a hydrophilic compound thereto.

46. The liposome according to claim 45, wherein the hydrophilic compound is a low molecular weight substance.

47. The liposome according to claim 45 or 46, wherein the hydrophilic compound rarely causes steric hindrance to the sugar chain and does not prevent proceeding of a reaction of recognizing the sugar chain by a lectin on the membrane surface of a target cell.

48. The liposome according to any one of claims 45 to 47, wherein the hydrophilic compound has a hydroxide group.

49. The liposome according to any one of claims 45 to 48, wherein the hydrophilic compound is an amino alcohol.

50. The liposome according to any one of claims 45 to 49, wherein the hydrophilic compound binds directly to the surface of the liposome membrane.

51. The liposome according to claim 45, wherein the hydrophilic compound of a low molecular weight has at least one OH group.

52. The liposome according to claim 45, wherein the hydrophilic compound is represented by the general formula (1):



where R1 denotes a C1 to C40 linear or branched hydrocarbon chain; R2 is absent or represents a C1 to C40 linear or branched hydrocarbon chain; X represents a reactive functional group directly binding to a liposome lipid or a linker protein or binding to a divalent crosslinking agent; and n is a natural number.

53. The liposome according to claim 45, wherein the hydrophilic compound is represented by the general formula (2):



where R3 denotes a C1 to C40 linear or branched hydrocarbon chain; R4 is absent or represents a C1 to C40 linear or branched hydrocarbon chain; H₂N represents a reactive functional group directly binding to a liposome lipid or a linker protein or binding to a divalent crosslinking agent; and n is a natural number.

54. The liposome according to claim 45, wherein the hydrophilic compound is represented by the general formula (3):



where R5 denotes a C1 to C40 linear or branched hydrocarbon chain; H₂N represents a reactive functional group directly binding to a liposome lipid or a linker protein or binding to a divalent crosslinking agent; and n is a natural number.

55. The liposome according to claim 45, wherein the membrane of the liposome and/or the linker protein are hydrophilized by covalently bonding a hydrophilic compound being a tris(hydroxyalkyl)aminoalkane to the membrane of the liposome and/or the linker protein.

56. The liposome according to claim 55, wherein the membrane of the liposome is hydrophilized by covalently bonding, to the membrane of the liposome, a hydrophilic compound selected from the group consisting of tris(hydroxymethyl)aminoethane, tris(hydroxyethyl)aminoethane, tris(hydroxypropyl)aminoethane, tris(hydroxymethyl)aminomethane, tris(hydroxyethyl)aminomethane, tris(hydroxypropyl)aminomethane, tris(hydroxymethyl)aminopropane, tris(hydroxyethyl)aminopropane, and tris(hydroxypropyl)aminopropane.

57. A liposome preparation prepared by encapsulating a medicinal drug or a gene in the liposome according to any one of claims 42 to 56.

58. The liposome preparation according to claim 57, wherein the medicinal drug is selected from the group consisting of medicinal drugs for tumors such as an anticancer drug based on an alkylating compound, metabolic antagonist, plant derived anticancer drug, anticancer antibiotic, BRM, cytokine, anticancer drug based on a platinum complex, immunotherapeutic drug, hormonal anticancer drug, and monoclonal antibody; medicinal drugs for the central nerve; medicinal drugs for the peripheral nervous system/sensory organ; therapeutic drugs for a respiratory disease; medicinal drugs for a circulatory organ; medicinal drugs for a digestive organ; hormonal medicinal drugs; medicinal drugs for a urinary/genital organ; medicinal drugs for external application; vitamins/analeptics; medicinal drugs for blood and body fluid; metabolic medicine; antibiotic/chemotherapeutic agents; medicinal drugs for medical check; anti-inflammatory agents; medicinal drugs for eye disorder; medicinal drugs for the central nervous system; medicinal drugs for the autoimmune system; medicinal drugs for the circulatory agent; medicinal drugs for lifestyle-related diseases such as diabetes and hyperlipemia; various oral, pulmonary, transdermal or transmucosal drugs; adenocortical hormones; immunosuppressive agents; antibiotics; anti-viral agents; neovascularization inhibitors; cytokines; chemokines; anti-cytokine antibodies; anti-chemokine antibodies; anti-cytokine/chemokine receptor antibodies; nucleic acid preparations involved in gene

therapy such as siRNA, miRNA, smRNA, antisense ODN and DNA; neuroprotective factors; and various antibody medicines.

59. The liposome preparation according to claim 57 or 58, being a preparation for peroral administration.

60. The liposome preparation according to claim 57 or 58, which is a parenteral preparation.

61. An anticancer drug comprising the liposome preparation according to claim 58, wherein the medicinal drug is a drug for a tumor.

62. The liposome preparation according to claim 61, wherein the medicinal drug is doxorubicin.

63. The anticancer drug according to claim 61 or 62, which is to be orally administered.

64. The anticancer drug according to claim 61 or 62, which is to be parentally administered.

65. A cosmetic composition comprising a liposome preparation prepared by encapsulating a cosmetic in the liposome modified by a sugar chain according to any one of claims 1 to 33.

66. The cosmetic composition according to claim 65, which is a preparation to be transdermally administered.

67. The cosmetic composition according to claim 65 or 66, wherein the cosmetic is vitamin A or vitamin E.

68. A food composition comprising a liposome preparation prepared by encapsulating a food in the liposome modified by a sugar chain according to any one of claims 1 to 33.

69. The food composition according to claim 68, which is a preparation for peroral administration.

70. The food composition according to claim 68 or 69, wherein the food is a nutritional supplement.

71. The food composition according to claim 69 or 70, wherein the food is vitamin A or vitamin E.

72. A cosmetic composition comprising a liposome preparation prepared by encapsulating a cosmetic in the liposome according to any one of claims 42 to 56.

73. The cosmetic composition according to claim 72, being a preparation for transdermal administration.

74. The cosmetic composition according to claim 72 or 73, wherein the cosmetic is vitamin A or vitamin E.

75. A food composition comprising a liposome preparation prepared by encapsulating a food in the liposome according to any one of claims 42 to 56.

76. The food composition according to claim 75, which is a preparation for oral administration.

77. The food composition according to claim 75 or 76, wherein the food is a nutritional supplement.

78. The food composition according to claim 76 or 77, wherein the food is vitamin A or vitamin E.